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EXAMINER	
GEMBEH, SHIRLEY V	

ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
11/29/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/578,452	GREINACHER ET AL.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-9 and 12-20* is/are pending in the application.

4a) Of the above claim(s) *5-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4 and 12-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/4/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

DETAILED ACTION

1. The response filed on **10/04/10** has been entered.

2. Applicant's arguments filed 10/4/10 have been fully considered but they are not deemed to be persuasive.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 1, 4-9 and 12-20 are pending in this office action, claims 5-9 are withdrawn based on the restriction requirement.

5. The objections of claims 10-11 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn due to the cancellation of the claims.

Information Disclosure Statement

6. The information disclosure statement (IDS) submitted on 10/4/20 is acknowledged and has been reviewed.

7. The rejection of claim 4 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn due to the amendment to the claim.

8. Claims 10-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn because the claims have been cancelled.

9. The rejection of claims 1 and 4 under 35 U.S.C. 101 because the claimed invention lacks patentable utility have been withdrawn because the claims have been amended or cancelled.

Rejections Maintained, but amended in view of Applicants amendment:

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicant should note that prophylaxis is interpreted as prevention therefore necessitating the rejection below.

Applicant argues on pages 9-10 of the remarks that 'Susman is a study comparing the effectiveness of two drugs over time in preventing second strokes. Susman says nothing about the use of the drug in the treatment of stroke compared to the prophylaxis of stroke. In addition, at page 2 of Susman, Dr. Ralph Sacco of the University of Miami and a member of the study group stated that "...the results still indicate that either of these drugs can be used to prevent second stroke," and this statement supports the use of the drugs in the prophylaxis of cardiovascular disease".

In response Applicant is missing the issue of 112-1 rejection, the claims are drawn to a method of treatment and /or prophylaxis of a cardiovascular treatment "wherein the treatment and/or prophylaxis is a treatment, primary prophylaxis and/or secondary prophylaxis is for acute coronary...".

Applicant is enabled for treating but not for prophylaxis of cardiovascular disease. Even though Applicant has cancelled the active compound dipyridimole discussed by Sussman prophylaxis of cardiovascular disease is still not enabled. For example congenital heart defects- a cardiovascular disease is one that cannot be prevented. In preventing coronary heart disease there are many factors one must consider, heart disease is due to cellular dysfunction, stemming from poor diet, inflammation, abnormalities in insulin function, liver dysfunction, aging and a host of other forms of dysfunction, therefore one cannot prevent cardiovascular disease. Susman discussed that even with medication patients had a second stroke (see page 2).

Additionally, the working example found on **pages 10-24** fails to reasonably correlate to prophylaxis of a wide variation of cardiovascular disease. Applicant's

omission of working examples does not enable one of ordinary skill in the art to treat the numerous amounts of diseases encompassed by the instant invention.

Applicant's arguments have been fully considered but they are not persuasive for the reasons made of record.

In Summary

Claims 1, 4 and newly added claims 19 and 20 stand/ and are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating acute coronary syndrome, angina pectoris, cardiac infarction does not reasonably provide enablement for prophylaxis of cardiovascular disease.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2nd 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

Nature of the invention.

The nature of the invention is directed to treating and/or prophylaxis of cardiovascular disease with the use of an inhibitor of the multidrug resistance protein (MRP4). As stated, however, claim 1 includes within its scope a wide variation of cardiovascular diseases that may or may not be prevented.

Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The quantity of experimentation needed is undue experimentation. One of ordinary skill in the art would first need to determine the type of conditions in other to carry out prophylaxis in the patient.

Amount of direction and guidance provided by the inventor.

The amount of direction or guidance present is not sufficient to show prophylaxis of a wide variation of cardiovascular diseases. The gap between the teaching in the specification of *in vitro* activity and *in vivo* is large enough to warrant thorough and compelling *in vivo* data especially in the absence of working examples demonstrating the full scope of prophylaxis of cardiovascular diseases.

Existence of working examples.

As discussed above, the working example found on **pages 10-24** fails to reasonably correlate to prophylaxis treatment of a wide variation of cardiovascular disease. Applicant's omission of working examples does not enable one of ordinary

skill in the art to treat the numerous amounts of diseases encompassed by the instant invention.

Breadth of claims.

Claim 1 is extremely broad due to the vast number of possible diseases encompassed by the instant invention.

Thus the current claims are not commensurate in scope with the limited guidance provided in the specification, and therefore, would require undue experimentation for the skilled artisan to reasonable discover how to make the currently claimed invention work.

Suggested language. Since the term "treatment" is a broad term, it will inherently cover therapies in which some protective function may also be present. Accordingly, the examiner recommends simply reciting method for "treatment" of cardiovascular disease.

New Rejections necessitated by amendment:

11. Claims 1, 14 and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claimed invention is drawn to methods of treatment and/or prophylaxis of a cardiovascular disease.....administering an inhibitor of MRP4 wherein the inhibitor is peptide, a peptide analog, an antibody, a peptidomimetic, a neutral or

anionic compound having a molecular weight of about 200-1000 daltons..... wherein the inhibitor of MRP4 is not an amphiphillic organic compound.

Therefore, the claims encompass a genus of molecules, e.g., "peptide, a peptide analog, an antibody, a peptidomimetic, a neutral or anionic compound having a molecular weight of about 200-1000 daltons...., wherein the inhibitor of MRP4 is not an amphiphillic organic compound, defined solely by its principal biological property, e.g., "wherein the inhibitor of MRP4 is not an amphiphillic organic compound", a peptide, a peptide analog etc is simply a wish to know the identity of any material with that biological property. Thus, while the specification appears to contemplate what is encompassed by wherein the inhibitor of MRP4 is not an amphiphillic organic compound there is insufficient written description encompassing a "peptide, a peptide analog, an antibody, a peptidomimetic, a neutral or anionic compound having a molecular weight of about 200-1000 daltons...., wherein the inhibitor of MRP4 is not an amphiphillic organic compound," because the relevant identifying characteristics of the genus such as structure or other physical and/or chemical characteristics of the "active ingredient" are not set forth in the specification as-filed.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant

> complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

Here, applicant has not described a reasonable number of members of the genus now claimed. The instant claims are often referred to as "reach-through" claims, where an applicant attempts to obtain patent protection on an invention not yet discovered. The Court of Appeals for the Federal Circuit addressed claims of this sort in great detail

in *University of Rochester v. G.D. Searle and Co.* (69 USPQ 2nd 1886, CAFC 2004). In *Rochester*, the Federal Circuit upheld the district court's ruling that patent claims which recited administration of compounds not disclosed, but rather to be identified in a screening assay, were invalid on their face. While the instant claims are drawn to methods of administering them, the situation is analogous to that in *Rochester*. Since the specification does not disclose to the public the structures of inhibitor of MRP4 is not an amphiphillic organic compound as claimed, it does not meet the written description requirement of 35 USC § 112, first paragraph.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 and 4 stand rejected and **new** claims 12, 14-15 and 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Heidland et al. (American Heart Journal 139(3) 2000, Mosby Inc.). The rejection is as follows necessitated by the newly added claims.

Heidland et al. teach treating cardiovascular disease (i.e., intracoronary stent placement or balloon angioplasty, myocardial infarct) with the active agent (i.e., dipyridamole, as required by instant claims 1, 4, 14 and 17, see page 1, under conclusion). Because Heidland teaches a method of treating cardiovascular disease dipyridamole and the specification when used as a dictionary teaches that dipyridamole is a neutral or anionic compound having a molecular weight of about 200-1000 daltons.

Since Applicant on page 4, lines 45 gave examples of a neutral or anionic compound having a molecular weight of about 200-1000 daltons it is reasonable that dipyridamole is an inhibitor of the multi-drug resistance protein MRP4 in platelets because as stated in the MPEP 2112.01"Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) and therefore is a cyclogenase inhibitor of a structural analog of a cyclic nucleoside (as required by instant claim 4).

With regards to instant claims 12, 15 because claims 14 and 17 that is further limiting recites that the compound is a neutral or anionic compound having a molecular weight of about 200-1000 daltons and dipyridamole as discussed supra is a neutral or anionic compound having a molecular weight of about 200-1000 daltons it is therefore reasonable that dipyridamole will inhibit multidrug resistance protein 4 mediated storage of adenosine diphosphate in a platelet and also inhibit ADP transport in a platelet because if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. With regards to the method comprising step of administering to the subject before or after stent implantation (as required by instant claims 1), Heidland specifically teach administering the drug after percutaneous transluminal coronary angioplasty and stent placement, see page 2.

In response to the previous rejection, Applicant argues that the claims as now amended have overcome the rejection.

In response, even though Applicant has amended the claims, and when the specification is used as guidance, the recitation of "wherein the inhibitor of MRP4 is a neutral or anionic compound having a molecular weight of about 200-1000 daltons" is taught by Heidland. Page 4, lines 26-35, describes "neutral or anionic compound having a molecular weight of about 200-1000 daltons" encompasses dipyridamole.

Therefore Heidland teaches the instant claim limitation and the argument is found not persuasive.

13. Claims 1, 4, 12-13 and 15-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Wallace (US Patent 6,476,037).

Wallace teaches a method of treatment of a cardiovascular disease in a subject wherein the cardiovascular disease is an angina (see col. 8, lines 1-3, as required by instant claim 18) having coronary artery bypass comprising administering zaprinast (see col. 3, lines 18-21 as required by instant claims 13 and 16, i.e., during stent implantation), wherein it is administered after coronary artery by pass (see col. 3, lines 45- 50, as required by instant claims 1).

With regards to instant claims 12 and 15 because claims 13 and 16 are further limiting, reciting the compounds that will comprise such function/characteristics it is therefore reasonable that zaprinast will inhibit multidrug resistance protein 4 mediated storage of adenosine diphosphate in a platelet and also inhibit ADP transport in a platelet because if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present.

14. Claims 1, 4, 12-13 and 15-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Jedlitschky et al. (Manuscript M005463200, 07/11/2000)

Jedlitschky et al. teach method of treating angina pectoris (see p41, as required by instant claims 1, 4) administering an inhibitor of MRP4 (i.e., MK571, as required by instant claims 1, 4, 13, 14,16, 18, 19, see page 15, 1st para, lines 5-12).

With regards to instant claims 12 and 15, it would be necessarily be expected that once the drug is administered it will inhibit adenosine di-phosphate transport in the platelet as required because administering the drug would necessarily result in contacting the platelets. Since there is no distinguishing procedure other than administering the drug, it is anticipated that it will have the same characteristics.

With regards to instant claim 20, the recitation "wherein if necessary for invasive intervention or therapy for severe hemorrhage exists in a subject , the inhibitor of MRP4 can be antagonized by transfusion of platelets"

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4 and 14-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heidland et al. (American Heart Journal 139(3) 2000, Mosby Inc.) in view of Wallace (US Patent 6,476,037) and further in view of Jedlitschky et al. (Manuscript M005463200, 07/11/2000) as evidenced by Reid et al. Molecular Pharmacology (2003), 63(5), 1094-1103).

Heidland et al. teach treating cardiovascular disease (i.e., intracoronary stent placement or balloon angioplasty, myocardial infarct) with the active agent (i.e., dipyridamole, as required by instant claims 1, 4 14 and 17, see page 1, under

conclusion). Because Heidland teaches a method of treating cardiovascular disease dipyridamole and the specification when used as a dictionary teaches that dipyridamole is a neutral or anionic compound having a molecular weight of about 200-1000 daltons. Since Applicant on page 4, lines 45 gave examples of a neutral or anionic compound having a molecular weight of about 200-1000 daltons it is reasonable that dipyridamole is an inhibitor of the multi-drug resistance protein MRP4 in platelets because as stated in the MPEP 2112.01"Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) and therefore is a cyclogenase inhibitor of a structural analog of a cyclic nucleoside (as required by instant claim 4).

With regards to instant claims 12, 15 because claims 14 and 17 that is further limiting recites that the compound is a neutral or anionic compound having a molecular weight of about 200-1000 daltons and dipyridamole as discussed supra is a neutral or anionic compound having a molecular weight of about 200-1000 daltons it is therefore reasonable that dipyridamole will inhibit multidrug resistance protein 4 mediated storage of adenosine diphosphate in a platelet and also inhibit ADP transport in a platelet because if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. With regards to the method comprising step of administering to the subject before or after stent implantation (as required by

instant claims 1), Heidland specifically teach administering the drug after percutaneous transluminal coronary angioplasty and stent placement, see page 2.

However Heidland fails to teach the specific inhibitor recited in claim 16, 19 and 20.

Wallace teaches a method of treatment of a cardiovascular disease in a subject wherein the cardiovascular disease is an angina (see col. 8, lines 1-3, as required by instant claim 18) having coronary artery bypass comprising administering zaprinast (see col. 3, lines 18-21 as required by instant claims 13 and 16, i.e., during stent implantation), wherein it is administered after coronary artery by pass (i.e., during stent implantation, see col. 3, lines 45- 50, as required by instant claims 1).

With regards to instant claims 12 and 15 because claims 13 and 16 are further limiting, reciting the compounds that will comprise such function/characteristics it is therefore reasonable that zaprinast will inhibit multidrug resistance protein 4 mediated storage of adenosine diphosphate in a platelet and also inhibit ADP transport in a platelet because if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present.

It is for this reason Jedlitschky is added.

Jedlitschky et al. teach method of treating angina pectoris (see page 15, lines 8-21, as required by instant claims 1, 4) administering an inhibitor of MRP4 (i.e., MK571, as required by instant claims 1, 4, 13, 14,16, 18, 19, see page 15, 1st para, lines 5-12) wherein MK571 inhibits MRP4 (see page 15, lines 8-12).

With regards to instant claims 12 and 15, it would be obvious that once the drug is administered it will inhibit adenosine di-phosphate transport in the platelet as required because administering the drug would necessarily result in contacting the platelets.

It would have been obvious to one of ordinary skill in the art to substitute the drug of Heidland with the drug of either Wallace or Jedlitschky 's drug (i.e., zaprinast or MK571) with a reasonable expectation of success because it is known in the art that these drugs are used for treating cardiovascular diseases and since zaprinast, diprimidamole, MK571are drugs that inhibits MRP4 (as evidenced by Reid et. al., see abstract) Therefore, one of ordinary skill in the art would have been motivated to substitute one MRP4 inhibitor for another with a reasonable expectation of success.

Therefore the claims would have been obvious to one of ordinary skill in the art at the time of filing the claimed invention.

16. No claim is allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, BRANDON FETTEROLF can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. V. G./
Examiner, Art Unit 1618
11/16/10

/Brandon J Fetterolf/
Supervisory Patent Examiner, Art Unit 1628